Paper No. 29

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte GREGORY S. ROBINSON

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Appeal No. 1997-1670
Application 08/098,942

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ON BRIEF

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Before ROBINSON, SPIEGEL, and ADAMS, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 8-15 and 23-24. Claims 25-42 stand withdrawn by the examiner as directed to non-elected subject matter and are not before us in this appeal.

Claims 8 - 15 and 23 - 24 read as follows:

8. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CACCCTGG[T]CTCACCGCCTTGG-3', (SEQ ID NO [5] 6).

9. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CATGGTTTCGGAGGCCCTC-3', (SEQ ID NO 3).

10. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CACCCAAGACACGCAG[CAG]AAAGT-3', (SEQ ID NO 4).

11. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-TCGTGGGTGCACGCCTGGGAC-3', (SEQ ID NO 2).

15. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-C[A]TGCCCCGGTCACCGCCTCGG-3', (SEQ ID NO: 11).

13. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CATGGTTTCGGAGGCCCCGA-3', (SEQ ID NO: 15).

14. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CACCCAAGACACGCAGAAAGT-3', (SEQ ID NO: 13).

12. (Amended) An antisense oligonucleotide having the [formula] sequence 5'-CCATGGGTGCACGCCTGGGAC-3', (SEQ ID NO:17).

23. (Amended) A method of [inhibiting VEGF expression in vitro [according to claim 16], wherein the antisense oligonucleotide is chosen from the group consisting of the oligonucleotide phosphorothioates 5'-CACCCTGG[T]CTCACCGCCTTGG-3', (SEQ ID NO [5] 6), 5'-CATGGTTTCGGAGGCCCTC-3', (SEQ ID NO 3), 5'-CACCCAAGACACGCAG[CAG]AAAGT-3', (SEQ ID NO 4), 5'-TCGTGGGTGCACGCCTGGGAC-3', (SEQ ID NO 2) and mixtures thereof.

24. (Amended) A method of [inhibiting VEGF expression in vitro [according to claim 16], wherein the antisense oligonucleotide is chosen from the group consisting of the oligonucleotide phosphorothioates 5'-C[A]TGCCCCGGTCACCGCCTCGG-3', (SEQ ID NO: 11), 5'-CATGGTTTCGGAGGCCCCGA-3',(SEQ ID NO: 15), 5'-CACCCAAGACACGCAGAAAGT-3',(SEQ ID NO: 13), and 5'-CCATGGGTGCACGCCTGGGAC-3', (SEQ ID NO:17).

The references relied upon by the examiner are:

Pederson et al. (Pederson) 5,149,797 Sep. 22, 1992

PCT Application (Foulkes)[1] WO92 13063 Aug. 6, 1992

Uhlmann et al. (Uhlmann), "Antisense Oligonucleotides: A New Therapeutic Principle," Chemical Reviews, Volume 90, No. 4, pages 543-84 (1990).

Tischer et al. (Tischer), “The Human Gene for Vascular Endothelial Growth Factor,” The Journal of Biological Chemistry, Vol. 266, No. 18, pp. 11947-954 (1991).

Claffey et al. (Claffey), “Vascular Endothelial Growth Factor,” The Journal of Biological Chemistry, Vol. 267, No. 23, pp. 16317-322 (1992).

Kim et al. (Kim), “Inhibition of Vascular Endothelial Growth Factor-Induced Angiogenesis Suppresses Tumor Growth In Vivo,” Nature, Vol. 362, pp. 841-43 (1993).

GROUND OF RECORD

The examiner having withdrawn the rejection of the appealed claims 12-15 and 24, under 35 U.S.C. § 112, first paragraph, at page 2 of the Examiner's Answer (Answer), the sole remaining ground of rejection for consideration in this appeal is the rejection of claims 8-15 and 23-24 under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Uhlmann, Peterson, Kim, Foulkes, Claffey, Tischer and page 4 of the applicant's specification.

We reverse the rejection under 35 U.S.C. § 103.

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[1] The examiner and appellant have limited their consideration to the file copy of the abstract of this reference. We, therefore, have limited our consideration of this reference to this abstract.

BACKGROUND

The invention is described by applicant, at page 9 of the specification, as being directed to antisense oligonucleotides which have been constructed and are targeted to bind nucleic acid sequences encoding Vascular Endothelial Growth Factor (VEGF) thereby blocking production of the expression of VEGF. VEGF is stated to play an integral role in angiogenesis associated with a variety of pathological conditions.

DISCUSSION

The rejection under 35 U.S.C. § 103

Claims 8-15 and 23-24 stand rejected under 35 U.S.C. § 103 as obvious over the combination of Uhlmann, Peterson, Kim, Foulkes, Claffey, Tischer, and page 4 of the applicant's specification.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant. Id. In order to meet that burden the examiner must provide a reason, based on the prior art, or knowledge generally available in the art as to why it would have been obvious to one of ordinary skill in

the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297, n.24, 227 USPQ 657, 667, n.24 (Fed. Cir. 1985). On the record before us, the examiner has not met the initial burden of establishing why the prior art, relied on, would have led one of ordinary skill in this art to arrive at the oligonucleotides of claims 8-15 and the uses thereof of claims 23-24. The examiner acknowledges that (Answer, paragraph bridging pages 6-7):

> [t]he difference between what is taught and instantly claimed is that although Uhlmann et al. and Peterson et al. teach the advantages of employing their oligonucleotides to inhibit expression of genes involved in disease conditions, they do not explicitly teach employing their construct to inhibit the VEGF expression.

The examiner cites Kim as teaching the inhibition of growth of tumors using monoclonal antibodies specific to VEGF to inhibit the activity of VEGF; Foulkes as teaching a method of inhibiting VEGF expression by employing antisense oligonucleotides directed against VEGF mRNA; Claffey as teaching the nucleotide sequence of murine VEGF and Tischer as teaching the nucleotide sequence of the human VEGF. (Answer, page 7). The examiner then concludes (id.):

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleotide sequence of the oligonucleotide constructs taught by either Uhlmann et al. or Peterson et al. to create antisense oligonucleotides directed against the VEGF nucleotide sequence in order to inhibit VEGF expression as taught by Foulkes et al. One would have been motivated to inhibit

> VEGF expression for the expected benefit of inhibiting tumor growth (taught by Kim et al.) and because VEGF was well known to be a tumor angiogenesis factor, as admitted by the appellants on page 4 of the specification.

What is missing from the examiner's discussion of the rejection is any facts or evidence which would have directed one or ordinary skill in this art to the specific oligonucleotides of claims 8-15 or the in vitro use of those oligonucleotides as claimed in claims 23-24. Neither Uhlmann nor Peterson teach antisense oligonucleotides that are related to the inhibition of VEGF expression. Only Foulkes provides any information relating to the inhibition of VEGF using an antisense nucleotide. However, the abstract of the Foulkes document, relied upon by the examiner, provides no information about the nature or make up of the antisense oligonucleotides described therein. To the extent that the combination of references may be argued to demonstrate that it would have been obvious to generally create antisense oligonucleotides directed against the VEGF nucleotide sequence in order to inhibit VEGF expression, more is required. The claims on appeal are directed to specific oligonucleotides defined by nucleotide sequence. In order to establish a prima facie case of obviousness within the meaning of 35 U.S.C. § 103 of the subject matter of the claims on appeal, the prior art must have provided sufficient information to direct one skilled in this art to that which is claimed, i.e., the specific oligonucleotides claimed in claims 8-15 or use thereof of claims 23-24. Thus, we find that the examiner has not provided the factual evidence which would reasonably support a

rejection of the claims on appeal under 35 U.S.C. § 103.

Where, as here, the examiner fails to establish a prima facie case of obviousness, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore the rejection of claims 8-15 and 23-24 under 35 U.S.C. § 103 is reversed.

CONCLUSION

The examiner's rejection of claims 3-6 and 8-10 under 35 U.S.C. § 103 as obvious over the combined teachings of Uhlmann, Peterson, Kim, Foulkes, Claffey, Tischer, and page 4 of the applicant's specification is reversed.

REVERSED

Douglas W. Robinson)
Administrative Patent Judge)
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Carol A. Spiegel) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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